REMARKS

Status of the Claims

Claims 1-66 are pending. Claims 18-66 were withdrawn from further consideration in response to a restriction requirement by the Examiner, under 37 C.F.R. §1.142(b).

In the present Response, claims 18-66 are cancelled, without prejudice; claims 7-11 and 17 are amended; and new claims 67 and 68 are added. No new matter has been added by the instant amendments. For example, support for new claims 67 and 68 can be found, *inter alia*, at page 3, lines 26-29. Thus, after entry of these amendments, claims 1-17 and 67-68 are presented for consideration.

Pursuant to the Office Action, claims 7-11 and 17-17 are rejected under 35 U.S.C. §112, second paragraph. Claims 1-12, 15, and 16 are rejected under 35 U.S.C. §102, for allegedly being anticipated by Lockhart *et al.* (Nature Biotechnology, vol. 14, pp. 1675-1680, 1996) (hereinafter "Lockhart"). Claim 13 is rejected under 35 U.S.C. §103 for allegedly being unpatentable over Lockhart in view of Anderson *et al.* ("Nucleic Acid Hybridization," IRL Press, pp. 98-99, 1985) (hereinafter "Anderson"). Claims 14 and 17 are rejected under 35 U.S.C. §103 for allegedly being unpatentable over Lockhart.

Issues under 35 U.S.C. §112, second paragraph

Claims 7-11 and 15-17 are rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The Patent Office alleges that claims 7 and 8 are indefinite because of the limitation "...a procedure comprising random priming, nick translation, amplification, or equivalent..." emphasis added. The Patent Office further alleges that claim 9 is indefinite because of the limitation "...the detectable label comprises Cy3 or Cy5 or equivalent..." emphasis added. Likewise, the Patent Office alleges that claims 10 and 11 are indefinite because of the limitation

"DNase enzyme, or equivalent..." emphasis added. The Patent Office is unclear as to what is meant by equivalent.

The Patent Office alleges that claims 7 and 8 are indefinite over an improper Markush group. Applicants have amended claims 7 and 8 to recite the members as a Markush group, thereby obviating these rejections.

The term "equivalent"

Merely to expedite prosecution, Applicants have amended claims 7-11 to remove the reference to the term "equivalent." However, Applicants submit that one of ordinary skill in the art, would be familiar with common laboratory techniques and products and would understand what is contemplated to be an equivalent to the methods for generating segments of target genomic nucleic acid, detectable labels, or fragmenting or digesting genomic DNA with enzymes. Equivalence (equivalent) is a term that is well-recognized by one of skill in the art as well as the Patent Office, for example, see MPEP 2183 and 2184. Applicants, in order to expedite prosecution of the application, have removed the term "equivalent," thereby, obviating these rejections. However, Applicants submit that the scope of the claimed invention encompasses equivalents of the exemplary methods and compositions in claims 7-11.

The phrases "defined part of" and "substantially an entire"

The Patent Office alleges that claim 15 is indefinite because of the limitations "...sequences representing a defined part of or substantially an entire chromosome..." emphasis added. The Patent Office alleges that the terms "defined part" of a chromosome and a "substantially entire" chromosome are unclear. The Patent Office also alleges that claim 16 is indefinite because of the limitation "...substantially an entire genome... ." The Patent Office alleges that it is unclear how many sequences would be necessary to have a "substantially entire" genome represented.

Applicants submit that the terms "defined part" and "substantially an entire," in the context of their use in the claims and specification, define the claimed invention with a reasonable degree of particularity and distinctness to one of ordinary skill in the art. It is well

recognized that the term "substantially" is often used in conjunction with another term to describe a particular characteristic of the claimed invention. See, *e.g.*, MPEP 2173.05(b)(D). "Substantially" is a descriptive term commonly used in patent claims to "avoid a strict numerical boundary to the specified parameter." *Ecolab, Inc. v. Envirochem, Inc.* 264 F.3d 1358 (2001). "Substantially" is given its ordinary meaning and is construed in light of the written description and file history as understood by one of ordinary skill in the art.

Applicants respectfully submit that the skilled artisan would know what was meant by "substantially" an entire chromosome or genome. For example, at page 3, lines 25-31, of the specification, exemplary embodiments of the invention include a sample target genomic nucleic acid with sequences having a defined fragment of a chromosome or substantially one or more entire chromosomes or substantially an entire genome. On reading the indicated passage, in light of the specification as a whole, one of ordinary skill in the art would understand that the claimed invention is directed to methods of generating a molecular profile of genomic DNA including the steps of providing a plurality of nucleic acid probes, providing a sample of target nucleic acids comprising fragments, and contacting the genomic nucleic acids to the probes. Claims 68 and 69 were added to claim additional embodiments of the claimed invention. Accordingly, one skilled in the art would know that any size of the sample target genomic nucleic acid, whether a partial chromosome, substantial or entire chromosome, or substantial or entire genome, is within the scope of the practice of the claimed invention. Thus, one of ordinary skill in the art would understand that the claimed invention contemplates use of the claimed methods with all variations in the size of the genome used, and that "substantially" is equivalent to "not quite 100%." Moreover, a "defined part" is any portion of a chromosome that has been chosen by the user. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 15 and 16.

The Patent Office alleges that claim 17 is indefinite because of the limitation "...the chromosomal or genome is derived from a human... ." The Patent Office is unclear what chromosomal part is derived from a human. Applicants have amended claim 17 to obviate rejection.

In light of the amendments and remarks set forth above, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 7-11 and 15-17 under 35 U.S.C. §112, second paragraph.

Applicants respectfully aver that both before and after the changes made in the instant amendment, the claimed invention was described in full, clear, concise, and exact terms and met all conditions for patentability under 35 USC §101, §112, et seq. Accordingly, the scope of the claims of any resulting patent (and any and all limitations in any of said claims) shall not under any circumstances be limited to their literal terms, but are intended to embrace all equivalents. Under no circumstances may these claims be interpreted as having been narrowed.

Issues under 35 U.S.C. §102

Claims 1-12, 15, and 16 are rejected under 35 U.S.C. §102(b), for allegedly being anticipated by Lockhart.

The legal standard for anticipation under 35 U.S.C. §102 is one of strict identity. To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention.

Lockhart discloses methods and tools for the direct monitoring of large numbers of mRNAs in parallel. Lockhart states that while the sequences of the human genome will soon become available, sequence information alone is insufficient for a full understanding of gene function, expression, regulation, and splice-site variation. To remedy problem, Lockhart has turned to mRNA research. Lockhardt discusses the development of an approach that is based on hybridization to small, high-density arrays containing synthetic oligonucleotides (See the abstract of Lockhart, page 1675.)

In contrast, Applicants' claimed invention is directed to methods of generating a molecular profile of genomic DNA, including, in one aspect, providing a sample of target nucleic acid comprising fragments of genomic nucleic acid. There is no teaching in Lockhart for using genomic DNA in its methods. Lockhart only discusses mRNA research. Accordingly,

claims 1-12, 15, and 16, which are all directed to a method of generating a molecular profile of genomic DNA, including the step of providing a sample of target nucleic acid comprising fragments of genomic nucleic acid, are not anticipated by Lockhart. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-12, 15, and 16 under 35 U.S.C. §102 for allegedly being anticipated by Lockhart.

Issues under 35 U.S.C. §103

Claim 13 is rejected under 35 U.S.C. §103 for alleged being unpatentable over Lockhart in view of Anderson. Claim 13 is directed to an exemplary stringent hybridization condition and depends from 12, which in turn depends from 1. Thus, claim 13 incorporates all the limitations of claims 1 and 12.

For a proper rejection under 35 U.S.C. §103(a), the references, either alone or in proper combination, must teach or suggest all the claim limitations of Applicant's claimed invention. Applicant will show that the deficiencies of Lockhart are not cured by Anderson. Accordingly, a *prima facie* case of obviousness has not been established and the rejection can be properly withdrawn.

As stated above, Lockhart is defective because, *inter alia*, it does not teach providing a sample of target nucleic acid comprising fragments of genomic nucleic acid. Lockhart also does not suggest or motivate one of ordinary skill in the art to utilize a sample of target nucleic acid comprising fragments of genomic nucleic acid, as in the claimed invention. Using genomic DNA instead of mRNA would render the methods and arrays of Lockhart unsatisfactory for its intended purpose, which is to use mRNA to study gene function, expression, regulation, and splice-site variation.

Anderson is cited to cure the deficiencies of Lockhart. The Patent Office states that Anderson discloses hybridization conditions for aqueous solutions.

However, Anderson does not cure the defects in Lockhart because it does not teach, suggest or motive one skilled in the art to utilize a sample of target nucleic acid comprising

fragments of genomic nucleic acid. Anderson does not cure the defects in Lockhart to teach or suggest methods for generating molecular profiles of genomic DNA by hybridization of a genomic DNA target to an immobilized nucleic acid probe comprising providing a sample of target nucleic acid comprising fragments of genomic nucleic acid labeled with a detectable moiety, wherein each labeled fragment consists of a length smaller than about 200 bases.

Accordingly, claim 1 is patentable because neither Lockhart nor Anderson, either alone or in proper combination, teaches all the limitations of the claims. Because claim 13 incorporates all the limitations of claim 1, claim 13 is also patentable. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 13 under 35 U.S.C. §103 for allegedly being unpatentable over Lockhart in view of Anderson.

Claims 14 and 17 are rejected under 35 U.S.C. §103 for allegedly being unpatentable over Lockhart. Claims 14 and 17 are directed to DNA, chromosomes, and genome from a human. Claims 14 and 17 depend directly and indirectly, respectively, from claim 1, thus incorporating all the limitations thereof.

As discussed above, Lockhart does not teach, suggest or motive one skilled in the art to utilize a sample of target nucleic acid comprising fragments of genomic nucleic acid, as in the claimed invention. Accordingly, Lockhart does not render claims 14 and 17 unpatentable. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 14 and 17 under 35 U.S.C. §103 for allegedly being unpatentable over Lockhart.

CONCLUSION

Applicants request that the Examiner reconsider the application and claims in light of the foregoing reasons and amendments and respectfully submit that the claims are in condition for allowance.

If, in the Examiner's opinion, a telephonic interview would expedite the favorable prosecution of the present application, the undersigned attorney would welcome the opportunity

to discuss any outstanding issues and to work with the Examiner toward placing the application in condition for allowance.

Attached is a marked-up version of the changes being made by the current amendment.

Applicants believe that, except for the extension of time fee, no additional fees are necessitated by the present Response. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050.

Respectfully submitted,

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Version with markings to show changes made

In the claims:

Claims 7-11 and 17 have been amended as follows:

7. (Amended) The method of claim 1, wherein the sample of target genomic nucleic acid is prepared using a procedure selected from the group consisting of [comprising] random priming, nick translation, and amplification[, or equivalent,] of a sample of genomic nucleic acid to generate segments of target genomic nucleic acid; followed by a step comprising fragmentation or enzymatic digestion, or both, of the segments to generate a sample of target genomic nucleic acid consisting of sizes smaller than about 200 bases.

8. (Amended) The method of claim 7, wherein the random priming, nick translation, or amplification[, or equivalent,] of the sample of genomic nucleic acid to generate segments of target genomic nucleic acid incorporates detectably labeled base pairs into the segments.

9. (Amended) The method of claim 8, wherein the detectable label comprises Cy3™ or Cy5™ [or equivalent].

10. (Amended) The method of claim 1, wherein the sample of target genomic nucleic acid is prepared using a procedure comprising fragmentation of a genomic DNA to sizes smaller than about 200 bases by DNase enzyme[, or equivalent,] digestion of the segments.

11. (Amended) The method of claim 1, wherein the sample of target genomic nucleic acid is prepared using a procedure comprising fragmentation of a genomic DNA to sizes smaller than about 200 bases by applying shearing forces sufficient to fragment genomic DNA followed by DNase enzyme[, or equivalent,] digestion of the sheared DNA.

17. (Amended) The method of claim 15 or 16, wherein the chromosome [chromosomal] or genome is derived from a human.

Claims 67 and 68 have been added.